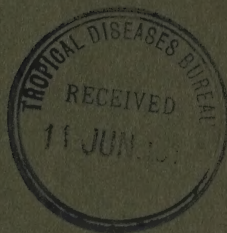
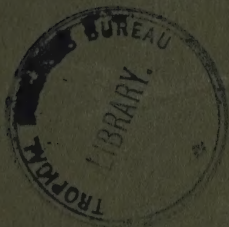


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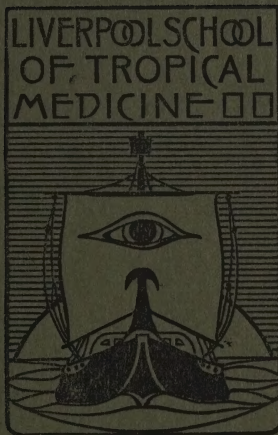
The Post-mortem Diagnosis of Yellow Fever

BY

HARALD SEIDELIN



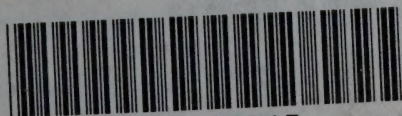
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THE POST-MORTEM DIAGNOSIS OF YELLOW FEVER

By HARALD SEIDELIN.

When a case has been under observation for yellow fever and terminates fatally, the clinician is naturally anxious that the pathologist should share the responsibility of the diagnosis. The pathologist is in a somewhat difficult position, because there is a widespread opinion that he ought to give his decision with absolute certainty, while one is not surprised if a clinician admits that he is in doubt.

In yellow fever it ought not to be so; the clinical diagnosis is, as a rule, easier than the post-mortem diagnosis considering that such a comparison can only be made in severe cases. In mild cases, where the clinical diagnosis encounters considerable difficulties, the anatomical diagnosis would probably be impossible if the opportunity of a post-mortem should be afforded through the accidental death, from some other cause, of a patient during a mild attack of yellow fever.

The consideration of both clinical data and anatomical findings may, of course, give more certainty than the clinical observation alone; consequently a post-mortem examination should always be made whenever possible.

Occasionally, the patients do not enter hospital until shortly before death; in such cases the clinical observation can hardly be sufficient, and autopsies will be the only means of diagnosis available.

Essentially the same conditions obtain at the post-mortem as during clinical observation, not a single symptom is pathognomonic, and in neither case can we expect to find any infallible test other than the demonstration of the specific micro-organism. Considering this, we had to admit, when discussing the clinical diagnosis, that cases may occur, the nature of which cannot be proved beyond doubt to everybody concerned. Theoretically, the same conditions prevail at the post-mortem examination, but in practice the situation is less unfortunate because nearly all fatal cases are typical.

The diagnosis is not always easy, but, I believe, possible in practically all cases if the observation is not limited to the macroscopic characters alone. Both microscopic and chemical tests may occasionally be necessary. As has been said already, there is no single pathognomonic lesion, but careful consideration of the alterations found in the digestive tract, liver, kidneys and myocardium, together with a negative result of the chemical tests for phosphorus, should suspicion of poisoning have arisen, will give a reasonable amount of certainty.

There is, however, no universal agreement on this point. Marchoux, Salimbeni and Simond (1903) are of opinion that the yellow colour of the liver, together with the cutaneous jaundice, justifies a diagnosis of yellow fever, but in a later paper Marchoux and Simond (1906) lay more stress upon the microscopic changes, although they do not describe them as specific. Mosny (1906), whilst considering the clinical diagnosis of yellow fever as comparatively easy, states that there are no anatomical lesions characteristic of this disease. Boyce (1911), on the other hand, considers the result of the post-mortem examination to be conclusive.

The general aspect of the body is very characteristic. There is a well-pronounced, though by no means always deep, jaundice and extensive livores, which generally are of a reddish purple colour.

Jaundice often develops only just before or even after death. For this reason, and because slight attacks without jaundice do not end fatally, this symptom is rightly considered to be of more constant occurrence at the post-mortem than in the clinic. The colour of the skin and conjunctivae is more or less intensely yellow, but not deep brown as in chronic jaundice. Certain mucous membranes, for instance that of the mouth, are of a somewhat deeper tint.

Jaundice was absent in five out of one hundred and fifteen autopsies performed by Azevedo Sodré and Couto (1901); death had occurred in all five cases at an early stage of the

disease, mostly from uraemia. It was also absent in ten out of sixty-three post-mortem cases observed by Alvarenga (quoted by Béranger-Féraud, 1890). Thus, the diagnosis of yellow fever may be made, even at the post-mortem, without the presence of jaundice.

Livid patches are most common and most extensive on the dependent portions of the body, that is to say, in most cases, on the back; but I have not infrequently observed them also on the sides of the abdomen and on the anterior surface of the femora.

Cutaneous haemorrhages are sometimes observed, principally on the legs.

Black or blood-stained fluid is seen escaping in nearly all cases from the mouth and often from the nose. This phenomenon, together with the yellow colour of the skin, produces a very striking impression.

When the opening of the body is proceeded with, the jaundice is seen to be very intense, first in the adipose tissue, and next on the serous surfaces. A pronounced yellow colour of the liquid in the serous cavities, especially the pericardium, is also observed, if a sufficient amount is present to make an appreciation possible.

We shall now discuss the alterations found in the different organs, not according to the sequence in which they are generally observed at the post-mortem, but according to their importance for the diagnosis.

The most characteristic alterations are, undoubtedly, found in the digestive tract and accessory glands.

Digestive organs. The mucosa of the tongue and that of the mouth and pharynx are covered with blood, and present a dark yellow or brownish-livid colour, and numerous fissures are often observed, especially on the tongue.

In some cases the oesophagus is not affected at all, but frequently there is a pronounced hyperaemia of its lower portion, and occasionally I have seen intense hyperaemia and numerous petechiae throughout its whole length.

The stomach contains in the vast majority of cases a haemorrhagic fluid which may be almost black, homogeneous

and of a tar-like consistence, or, more frequently, watery or mucous, with black particles in suspension. These particles are often extremely small and numerous, in which case the comparison with coffee grounds suspended in water is very appropriate; or they may be somewhat larger and then generally scarce, thus producing the characteristic aspect, which has given rise to the name of 'alas de moscas,' when seen in the vomit.

If all the free liquid has been vomited during life, there will be found only a muco-sanguinolent mass covering the stomach wall more or less completely; even this covering may be missing and then the only signs of haemorrhage are the ecchymoses and erosions found in the mucous membrane proper.

The black liquid has nearly always an acid reaction, and the presence of haemoglobin can be demonstrated by the tincture of guaiac and turpentine test.

Quite occasionally, almost pure, liquid or clotted, blood may be found in the stomach; on the other hand, in rare cases a bile-stained or colourless fluid may be present without any trace of blood at all. It is important to remember that such cases do exist, since the opinion prevails, and is sometimes expressed in text-books, that the presence of black stomach-contents is a *conditio sine qua non*, for the diagnosis of yellow fever. Such contents are truly of very frequent occurrence and exceedingly characteristic, when present, but they are all the same not invariably observed. The absence of haemorrhagic fluid makes one hesitate to accept a diagnosis of yellow fever; still, it does not disprove it.

Blair (1850) found black contents in 79 and blood in 2 cases out of a total of 97, Bérenger-Féraud (1890) encountered blood in some form or other in 484 out of 551 autopsies, and I have observed the presence of liquid containing blood in 21 out of 22 autopsies.

The mucous membrane is oedematous, and there is an abundant vascular injection, especially in the region of the lesser curvature. Petechiae seem to be a constant feature

when death has taken place during the acute stage, but absence of both congestion and petechiae is to be expected in the comparatively rare cases in which the patient has died at a later stage from cardiac failure.

More extensive haemorrhages and ulcerations are less common; the latter evidently originate in haemorrhagic foci, as I have been able to demonstrate on several occasions, and seem to depend entirely on the presence of such. It is, therefore, but natural that their size corresponds, within certain limits, to that of the haemorrhages, though large ulcerations are exceedingly rare. Only in one case have I observed an ulceration with a diameter of nearly 1 cm.

It is well known that gastric ulcers may, experimentally, develop in the course of a few days, and there is no reason why the same should not occasionally happen in yellow fever, where the existence of haemorrhagic foci in the mucosa and the probably continuous presence of acid liquid in the interior of the stomach would seem to favour such a process. There is nothing to disprove that such an ulcer may depend on pathological processes belonging essentially to yellow fever, and consequently there is no reason why its presence should be explained by the casual coincidence of an ordinary *ulcus ventriculi* with yellow fever, or even be used as a decisive argument against the latter diagnosis.

In the first part of the duodenum, conditions very similar to those obtaining in the stomach are observed. The mucosa presents hyperaemia and haemorrhages, and the contents have identically the same characters as the gastric contents; it is not easy to say whether they represent simply the gastric contents after their passage through the pylorus, or whether additional haemorrhages have taken place from the duodenal vessels. The intramucous haemorrhages have, in my cases, always been less numerous in the duodenum than in the stomach. In the lower part of the duodenum the affection vanishes rapidly, and is only in rare cases continued for a certain distance into the jejunum.

In the remaining portions of the small intestine there may be observed hyperaemic patches and more or less numerous

small haemorrhages, but these parts of the bowel are seldom affected to a great extent, and may be entirely uninvolved. The lesions, when present, are always very irregularly distributed.

The last few centimetres of the ileum are, again, more frequently the seat of pronounced alterations, the intensity of which rapidly increases on approaching the ileo-caecal valve.

In some cases there is a considerable swelling of both the solitary lymph-follicles and Peyer's patches.

In the large bowel there is, with great frequency, diffuse hyperaemia and oedema, and some portions of the mucosa may be remarkably like that of the stomach. Minute ulcerations may also be present. In fact, I have repeatedly seen severe lesions of nearly the whole extent of the colic mucosa and, contrary to the statements of most authors, I have the impression that the colon is, as a rule, much more severely affected than the jejuno-ileum. The alterations of the large bowel are often most pronounced in the caecum, colon descendens and rectum.

There is often a considerable amount of mucus present in the intestinal contents of both the large and small intestine, as well as in the stomach.

The irregular distribution of the lesions and the catarrhal condition of the mucosa of the digestive tract, together with the micro-cellular infiltration which is found on microscopic examination, are strong points in favour of the inflammatory nature of the whole affection and, consequently, also of the hyperaemia which is such a prominent feature amongst the phenomena observed in these organs. Another theory, which has been adopted by Carroll (1905), is to explain the hyperaemia as the result of a stasis in the portal system, due to compression of the fine intrahepatic ramifications of the vena portae. Were this the case, one would expect to find a more equal distribution of the hyperaemia and no inflammatory condition of the mucous membrane. It is hardly conceivable that the swelling of the liver-cells should produce such a high degree of stasis, and the microscopic

aspect of the liver is not one which would warrant a similar conclusion being drawn, as we shall see directly; neither does it seem necessary to adopt a particular explanation for the hyperaemia of the digestive tract when hyperaemia and haemorrhages are such prominent features of the disease.

The liver is of about normal size and weight. The surface is smooth, and the serous capsule preserves its normal glistening aspect. The colour may be uniform, yellow, but more frequently there is an irregular distribution of yellowish patches on a dark purple ground. In rare cases the whole organ is of a dark brown or purple colour. There is some vascular injection, which causes the anatomical structures to be slightly more visible than in the normal liver. Small haemorrhages may be seen through the serosa. The consistence is nearly always diminished and, occasionally, the organ may be quite soft and pasty, and in this case visible marks remain after pressure with the finger.

When an incision is made into the organ, the variations in consistence are well noted, and on the cut surface details of colour and design are observed similar to those seen on the outer surface. If the incision is made with a dry knife, fat is often deposited on its blade, a phenomenon which is only observed in cases of advanced fatty metamorphosis. The amount of fat contained in the liver may be so enormous that a fragment of the organ may float in water.

The cut surface is dry and little or no blood oozes from it, in the case of pale yellow livers; but in the comparatively few cases of congestion free bleeding takes place.

The alteration of the liver is certainly the most constant and one of the most typical post-mortem findings.

If both the typical hepatic lesion and haemorrhagic gastritis are present the diagnosis may be considered established.

If, on the other hand, the macroscopic appearances of the liver do not seem quite typical, the microscopic examination of carefully selected specimens may throw light on the question.

The microscopic characters of the liver are variously described, and the disagreement between the descriptions of different authors probably depends on differences in the material with which they have worked. In fact, the examination of a number of livers from yellow fever cases reveals very considerable variations in the histological aspect.

The one constant and prominent feature is the fatty metamorphosis which is found more or less developed in all livers.

In some cases this alteration completely dominates the picture. In every hepatic cell several fat drops of different size are seen, some of which are very large; they may completely obscure the view of the nucleus and other cell-structures. In some cases one gets the impression that the same total amount of fat may be present as in a fully developed case of so-called fatty infiltration of the liver, but the distribution is different. Whilst in the fatty infiltration the fat is contained principally in the cells occupying the peripheral parts of the lobules, we have in the yellow fever liver practically all cells affected to almost the same degree. Moreover, we do not find here the enormous fat drops which are seen in typical infiltration, where a single drop often occupies a whole cell and distends it considerably. The cells of a yellow fever liver may also be distended, but then they contain several fat-drops each, with intervening protoplasmic elements. The aspect is similar to that obtaining in phosphorus-poisoning, and closely corresponds to the classical descriptions of fatty degeneration, only representing an extreme degree. Modern investigations tend to show that in all cases of fatty metamorphosis the fat is introduced into the cell from without, i.e., by infiltration, and that, consequently, fatty degeneration in the old sense of the word does in reality not exist. The fact remains, however, that there are different histological characters which seem to indicate the existence of two kinds of metamorphosis, as described by earlier writers, no matter what the differences between them may be. The yellow fever liver corresponds well to the characters

of a degenerative metamorphosis, also in the sense that the affection evidently represents a much more serious interference with the function of the cell than that produced in a case of typical fatty infiltration. A complete destruction of the cell does not take place, since the nucleus, as a rule, stains fairly well, as can be seen in specimens of the same livers in which the fat has not been stained. Alterations similar to those observed in the liver cells, *sensu strictiori*, can be seen to a lesser degree in the epithelia of the bile-ducts, and also in the endothelia of the blood vessels.

In other cases the fatty metamorphosis is just as extensive, but the cells present a different aspect. Instead of a small number of larger drops the protoplasm is seen to contain an enormous number of minute fat-granules. These granules are distributed throughout the whole protoplasmic body, but the nucleus and some protoplasma-structures can still be distinguished, even in preparations in which the fat is stained. Fat-granules are often seen close to the nucleus, but I have never been able to demonstrate their actual presence in the interior of the nucleus.

In many cases the fatty metamorphosis is practically the only alteration of any importance; in such cases there may be, as an additional phenomenon, a slight microcellular infiltration around the vessels in the portal spaces. But, more frequently still, there are other important phenomena besides the fatty metamorphosis. Such phenomena are: necrobiosis, hyperaemia and cellular infiltration. Necrotic alterations may be observed in cells, in which there is also advanced fatty metamorphosis, or both phenomena together may have attained such a degree that only masses of detritus are left, representing groups of cells, and alternating with groups of fat-containing cells. The hyperaemia macroscopically shows an irregular distribution, but is rather diffuse in its histological relations. There is especially no definite localization inside the hepatic lobule. If anything, it appears to me more pronounced in the central portions of the lobules, around the hepatic vein, than in the neighbourhood of the portal veins. In fact, it may be

difficult to recognize the central vein amongst the numerous other spaces filled with blood. The cellular infiltration corresponds chiefly to the portal spaces, but may be continued into the interior of the lobules. It may be very abundant, and always consists essentially of lymphocytoid cells; polymorphonuclear leucocytes are observed in very small numbers only.

Bile-pigment is present and often abundant, both in the hepatic cells and in the stroma cells. When sublimate-fixation has been used, it is generally green, the bilirubin having been converted into biliverdin.

Fatty infiltration on the one hand, necrosis, hyperaemia and, to a lesser degree, cellular infiltration on the other, are often so overwhelming that practically no liver cells seem to remain intact, and it is hardly intelligible, how the gland has been able to continue its function. This is a point of the greatest pathological importance, as the modern tendency is to explain all kinds of jaundice as hepatogenous. In yellow fever we have no stoppage of the bile-flow into the intestine, a fact which is evident not only because no hindrance can be found, but also because the intestinal contents are always bile-stained. In one case only have I seen rather pale, though not clay-coloured faeces.

Notwithstanding this, bile-pigments are deposited in the tissues in considerable quantities. According to modern theories of the pathogeny of jaundice, these pigments, as well as those which pass into the intestine, are supposed to be of hepatic origin. In this case, the liver, in spite of its highly damaged condition, would seem to have performed not only the ordinary amount of work, but even an excess. Such an assumption seems, however, quite incompatible with the histological aspect of the liver. I am at present studying these phenomena and hope to report my results at some future date.

Another point of importance requires a short discussion. Azevedo Sodré and Couto (1901) describe a pronounced anaemia of the liver tissue and seem never to have observed hyperaemia, which is so well described by Carroll (1905). So far I quite agree with Carroll, but when he looks upon

the matter as essentially a stasis in the portal system, I cannot follow him. In my cases of intense hyperaemia all vessels were engorged, from the central veins, through the capillaries, to the ramifications of the vena portae, and I have not been able to convince myself of any swelling of the endothelial cells sufficient to account for a portal stasis. I find also that Carroll himself mentions that the central veins are frequently engorged, an occurrence which is not likely to be met with in cases of portal stasis. All this considered, there seems to be a lack of foundation for the explanation that the hyperaemia which is always found in the digestive tract should be due to stasis in the portal system.

The microscopic examination of the liver may be of considerable help in establishing the diagnosis of yellow fever, if the macroscopical post mortem appearances do not seem sufficiently characteristic. In this case stress should be laid upon the demonstration of the fatty metamorphosis as the most characteristic phenomenon, and for this purpose the use of a freezing microtome and staining of the sections with Sudan III is necessary. Osmium methods give excellent preparations, but are of little use for a rapid diagnosis.

The bile-ducts are permeable, and the gall-bladder contains generally a small quantity of thick, mucous, dark yellow bile, but in a few cases I have found it distended with greenish or almost black, liquid bile. Rochoux (1828) mentions a case in which the gall-bladder contained bile mixed with blood.

The pancreas is often slightly enlarged and of considerably diminished consistence and pale colour, but it may also present, macroscopically, a normal aspect. The microscopic examination shows phenomena similar to those observed in the liver. Fatty metamorphosis seems to be of constant occurrence; the alteration is distributed equally over the whole organ, fine granules of fat being present in nearly all the epithelial cells. Necrosis may also be present, but is not constant, and hyperaemia is not even common.

The islands of Langerhans show alterations similar to

those observed in the cells belonging to the true secretory system, but less pronounced.

The pancreas is, as far as my experience goes, constantly and severely affected in yellow fever, but the alterations do not appear to be very characteristic and are consequently of little diagnostic value.

Urinary organs. The kidneys are slightly enlarged. The serous capsule can easily be detached from the organ, and the parenchyma then bulges forward as if relieved from a certain amount of pressure. The surface is smooth and the vascular design prominent; the colour is dark red or cyanotic, with irregularly shaped, large and small, yellow patches. The difference in colour becomes more visible and the yellow parts more predominant when the kidney is bisected. There is intense vascular injection corresponding to the bases of the pyramids, whilst their apices are generally yellow; in the cortex the yellow colour is more irregularly distributed, and it is sometimes observed that the consistence of the yellow portions is diminished. In a few cases I have found the whole kidney somewhat friable. Small haemorrhagic spots are often seen in the cortex.

The mucosa of the renal pelvis presents vascular injection and frequently haemorrhages.

The ureters show a slight hyperaemia, but no other alteration.

Also the mucosa of the bladder may be slightly hyperaemic, but often presents a normal aspect. The bladder generally contains a small quantity of urine which it is important to collect for examination. In these cases the urine is dark and gives strong reactions when tested for albumin and bile-pigments. Occasionally, there is no urine at all and, on the other hand, in rare cases there is a fairly large amount. In the latter case the quantity of albumin present may be less considerable than when the amount of urine is very small.

A microscopic examination of the kidneys is occasionally made at once at the autopsy and may, together with that of the liver, prove of diagnostic value. An extensive fatty

metamorphosis is, also in the kidney, the most characteristic feature, but it differs considerably, in various characters, from that observed in the liver. It is very irregularly distributed, being most pronounced in the portions which have been macroscopically described as yellow patches, but in some places it is altogether absent. In the parts most severely affected there is a large number of small fat-granules in all the epithelial cells of the convoluted tubules; occasionally a single larger drop of fat may be seen in a cell, besides the small granules, but large drops are never abundant, contrary to the conditions observed in the liver. In the same situations in the kidney, fatty metamorphosis is, as a rule, present in the epithelia of the straight tubules also, but less developed; in the lining cells of Bowman's capsules it is absent or but slightly pronounced. In some parts a more or less advanced necrosis has taken place; the nuclei stain badly or have disappeared entirely, the cell limits are vanishing, and sometimes irregular masses of detritus and fat-granules are the only remains of the epithelial layer of the tubules. Thus, deeply affected and almost undamaged histological elements are seen side by side.

Hyperaemia is often pronounced, but its distribution is irregular; small haemorrhages are also common. A slight microcellular, perivascular infiltration is seen in most specimens. Casts are often seen in the tubules.

Durham (1902) and Boyce (1911) lay stress upon the dilatation of Bowman's capsules, which is frequently seen; but in my experience this phenomenon has not been more pronounced than in other cases of acute nephritis.

The whole picture is that of an acute nephritis with intense degeneration of the parenchyma.

For rapid examination of the kidney the same technique is employed as in the case of the liver.

The *spleen* is not severely affected in yellow fever. It is of normal size or slightly enlarged; its colour and consistence are normal. The microscopic examination shows, apparently in all cases, hyperaemia, and this may account for a slight

enlargement. But any considerable enlargement of the spleen in a typical case of yellow fever is an indication, either of coincidence with some other disease, or of secondary infection.

The *lymph-nodules* in different parts of the body were found by Durham (1902) to be enlarged, but other observers mention only enlargement of the mesenteric nodules, which may be easily explained by bacterial invasion from the intestine, as microbes would readily pass through the damaged mucosa.

Circulatory system. The intima of the large blood vessels show very clearly the existence of jaundice, which is also visible, as a rule, on both the pericardial and endocardial surfaces of the heart. Azevedo Sodré and Couto (1901) describe aortitis ulcerosa, but no similar affections have been observed by other authors.

The heart is generally distended and flabby. Subpericardial haemorrhages are very common, and may either be quite small or somewhat larger and often confluent. Intramural and subendocardial haemorrhages are occasionally seen. The myocardium is of diminished consistence and often friable; its colour is pale, and it shows irregular yellow streaks and spots. Microscopically, fatty metamorphosis of the muscle-fibres is observed, though often less developed than one would expect, considering the macroscopic appearance. In this case microscopic examination is of less diagnostic value than direct observation.

Azevedo Sodré and Couto (1901) have described endocarditis as a constant phenomenon, but no other observers have found it. Personally, I have never seen endocarditis in yellow fever, and feel strongly inclined to consider its presence as an indication of secondary infection. That secondary infections seem to occur, with unusual frequency, in yellow fever cases in Brazil, is a remark which I have already made in an earlier paper (1911).

Some of the other characters, described by the same Brazilian authors, are evidently of no importance whatever, namely, 'tendinous patches' on the anterior surface of the

heart and excess of subpericardial fat; both are lesions of a chronic nature and can certainly not develop during the course of an acute disease like yellow fever.

There may be a slight increase of the pericardial liquid.

Nervous system. In my own cases, only the brain has been examined. The only appearance which struck one was a considerable congestion of the meninges and, in some cases, of the cerebral cortex. Haemorrhages in the cerebral substance have been described, and furnish together with the hyperaemia satisfactory explanation of the nervous symptoms so frequently observed in yellow fever.

From a diagnostic point of view the examination of the nervous system is of little importance in yellow fever.

Respiratory organs. Subpleural haemorrhages are frequent. The lungs show considerable congestion, which may be very intense in the inferior lobes. I have not seen pneumonic infiltrations, and their occurrence is also, according to other writers, uncommon. When present, they are probably not due to the action of the yellow fever virus, but to secondary bacterial infections.

No characteristic lesions of the air-passages are observed.

Ductless glands. Several authors have described fatty metamorphosis of the suprarenal capsules; I have also seen hyperaemia of these organs, but they do not appear to be constantly affected and the lesions are, at any rate, not specific.

In a few cases I have seen hyperaemia and slight enlargement of the hypophysis cerebri.

No characteristic alterations of the thyroid body have been observed.

Marchoux and Simond (1906) found fatty metamorphosis in both hypophysis and thyroid body.

Genital organs. The uterine mucosa is congested, and blood is present in the uterine cavity. This corresponds to the apparently constant occurrence of metrorrhagia during yellow fever.

The ovaries and testicles do not present macroscopically visible alterations; but microscopic examination has shown in

several of my cases well marked fatty metamorphosis, as has been observed also by Marchoux and Simond. These authors found also similar lesions in the prostate gland and in the urethral epithelium.

DIFFERENTIAL DIAGNOSIS

Malaria. Clinically there exists a good deal of resemblance between light attacks of malaria and of yellow fever. At the post mortem there will be less probability of mistaking one of these infections for the other. The enlargement of the spleen in malaria and, if necessary, a rapid microscopic examination of smears from this organ, will prove the malarial infection and thereby, in most cases, solve the question. The possibility of mixed infection must, however, be admitted; death may be caused by yellow fever in an individual infected with malaria. Thus arises the necessity of differentiating between an acute attack of malaria perniciosa with gastro-intestinal affection, and yellow fever complicated with malaria. The presence of haemorrhagic, especially black, fluid in the stomach and duodenum is in favour of yellow fever, but in the absence of such, the other phenomena may leave us in doubt. Inflammation of the mucosa and petechiae may be observed in pernicious malaria also, though more diffusely and irregularly distributed than in yellow fever, in which disease their localization to the stomach and duodenum is characteristic. The examination of the liver will often be more decisive. This organ is very dark, the seat of congestion and pigmentation, in acute malaria, but yellow and fatty in yellow fever. As mentioned already, a microscopic examination of the liver for the presence of fat may be of use.

In *blackwater fever* the examination of the urine, if any can be obtained from the bladder at the post-mortem, will decide the diagnosis. Moreover, the kidneys show a higher degree of congestion and less fatty metamorphosis than in the case of yellow fever, whilst, on the other hand, the gastro-intestinal and hepatic alterations are absent or but

little pronounced. Also here, the macroscopic and microscopic characters of the liver are of great value, as intense fatty metamorphosis, accompanied by necrotic and inflammatory phenomena, is not typical of haemoglobinuric fever.

Acute yellow atrophy of the liver. The anatomical lesions observed in this affection have many points of resemblance with yellow fever. In fact, in cases of yellow fever, in which the liver alterations dominate the picture, the stomach being less affected, it would be difficult to exclude the possibility of acute yellow atrophy, should no clinical data be available. Even a brief summary of the principal clinical facts would be useful, since the post-mortem findings would always point to a strong probability in one direction or the other. It may, therefore, be justifiable to consider jointly the clinical and pathological aspects in such cases. In both diseases haemorrhages may occur in various tissues, also apart from the digestive tract. Acute nephritis and degeneration of the myocardium are likewise lesions common to both affections. The size of the liver *may* be slightly reduced in yellow fever, and is not always much reduced in acute atrophy; fatty metamorphosis and necrotic alterations are essential phenomena in both. The duration of the disease would in such a case be of great importance for the diagnosis; an attack of yellow fever, in which the hepatic lesions were severe, but the gastric affection only slightly pronounced, might have lasted for a week, but probably not much longer, whilst death in a case of acute yellow atrophy would not have taken place before the end of the second week.

A considerable quantity of black stomach content would characterize the case as one of yellow fever, but the presence of a small amount of blood-stained fluid would not settle the question definitely, since the possibility of some bleeding taking place from the gastric mucosa in acute atrophy cannot be denied. Haemorrhages *in* the mucosa would be still less decisive. If yellow fever, a case with pronounced gastric affection would have run its course in less than a week, whilst, if acute atrophy, it would have

lasted considerably longer. The temperature would probably have been higher in yellow fever.

The few fatal cases of *Weil's disease*, which have been reported, presented similar lesions at the autopsy, to those of acute yellow atrophy; also haemorrhages in the gastric mucosa have been described. The joint consideration of clinical and post-mortem findings is likewise valuable and sometimes necessary, in order to differentiate this affection from yellow fever.

It cannot be denied that even with a full clinical history and a detailed post-mortem record one might occasionally hesitate in pronouncing a definite opinion, when called upon to differentiate a case of yellow fever from these two forms of icterus gravis. There is nothing of failure in this admission; we all know that the diagnosis of the first case of cholera or plague in a locality is, as a rule, not made before the presence of the specific micro-organisms has been proved. We shall undoubtedly arrive at the same point in yellow fever.

Hepatitis acuta has sometimes been diagnosed in cases, which other observers have considered as yellow fever; but in cases deserving the diagnosis of hepatitis one would expect to find the liver enlarged and also, as the cause of the liver affection, severe inflammatory lesions in the intestine.

Acute poisoning. In phosphorus poisoning there may be found an aspect of the liver similar to that in yellow fever cases, and there may also be haemorrhagic gastritis. If clinical data are available, there will seldom be any necessity of differentiating between this affection and yellow fever at the post-mortem table. Should the question, however, arise, the chemical analysis of the stomach contents will be decisive.

The same applies to arsenical poisoning also; but the question of this affection is less likely to be brought forward, as the similarity of its pathological lesions with those in yellow fever is less pronounced than in the case of phosphorus poisoning.

The anatomical lesions described in fatal cases of

poisoning with fungi present, according to Dixon Mann (1908), a striking resemblance to those observed in yellow fever, but diagnostic difficulties are not likely to arise, as the clinical symptoms are different and the etiology will generally be known. However, it is well to remember that here lies a possibility of mistake.

Otto (1907) says that the aspect of the stomach in yellow fever cases may be very similar to that observed in potassium cyanide-poisoning, but in reality the question of differential diagnosis does not arise, since the anatomical lesions of other organs are quite different. It is of interest that an alkaline reaction of the stomach contents must be expected in cases of this poisoning, according to Dixon Mann (1908), whilst it is nearly always acid in yellow fever cases, as mentioned before.

Acute gastro-enteritis, which plays some rôle in discussions on the clinical diagnosis of yellow fever, is also mentioned occasionally as a possibility at the post-mortem. Few pathologists would, however, accept that diagnosis without further qualification, when such severe lesions are present as those described in yellow fever.

Amongst the ulcerative processes which are observed in the stomach, the ordinary gastric ulcer would hardly be introduced into a discussion on the diagnosis of yellow fever, but superficial erosions, as described by Dieulafoy and others, might well be considered. The anatomical conditions in such cases differ considerably from those observed in yellow fever, in that hyperaemia and ecchymoses may be absent or but slightly developed, whilst in yellow fever erosions are seen only in cases with severe haemorrhagic gastritis. The simple erosions do not cause death except by acute haemorrhage, and the autopsy in such a case would show the presence in the stomach of a considerable amount of pure blood, contrary to what we have seen to be the case in yellow fever; moreover, no alterations of liver and kidney are observed similar to those in yellow fever.

I have never performed the autopsy in a case of yellow



fever in which death had taken place, during convalescence, from *heart failure*. If a deduction can be made from the clinical symptoms, it might occasionally be impossible to make the anatomical diagnosis, as the organic lesions would probably have lost their characteristic appearance in about a week's time after the fever had subsided. The myocardium would undoubtedly be found severely affected, but the aspect could not be expected to differ from that which would have been observed had the fatal issue been brought about by the same cause, heart failure, during the course of another infectious disease, as typhoid fever or diphtheria.

The liver would probably be the organ which, more than any other, would still show marks of severe lesions. I have repeatedly observed mitotic figures in liver cells in yellow fever cases, even in a most severely affected organ, when death had taken place at the height of the disease. In late cases one would expect to find active regenerative phenomena.

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